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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/030,740	03/27/2002	Xavier Nassif	1721-43	8255

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EXAMINER	
BASKAR, PADMAVATHI	

ART UNIT	PAPER NUMBER
1645	15

DATE MAILED: 11/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/030,740	Applicant(s) NASSIF ET AL.	
	Examiner Padmavathi v Baskar	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *6-16, 18 and 20-24*, _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,17 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's response to restriction in Papers N0: 11 (9/8/03) is acknowledged. Claims 1-24 are pending in the application.

Election

2. Applicant's election Group I, claims 1-5 and 17 and 19, drawn to polypeptide with respect to FhaB, SEQID.NO: 28 with traverse of in Paper # 11 is acknowledged.
The traversal is on the grounds that the examination of all open reading frames would not be an undue burden on the examiner. Therefore, reconsideration and withdrawal of the restriction requirement is requested.

This is not found persuasive because the examiner clearly established lack of unity between groups including open reading frames in paper # 10. As discussed in earlier office action, the common generic special technical feature does not link the DNA and polypeptide since they do not share a common structure or function or property as DNA is made of nucleic acids and polypeptide is made of amino acids. Thus, these two products are not linked by the common generic special technical feature as defined by PCT Rule 13.2. Additionally, the expression special technical features shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. However, SEQ.ID.NO: 66, 68 and 72 TolC ORF of N.meningitidis are anticipated by the prior art Accession number: AF 121772 and thus there is no special technical feature exists among groups or ORFS. Therefore, it does not constitute a special technical feature by definition and hence lack of unity is present.

3. Claims 6 –16, 18 and 20-24are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 11.

4. Claims 1-5, 17 and 19 will only be examined to the extent they read on the elected invention of SEQ ID N0: 28 or FhaB polypeptide, all other sequence identifiers are withdrawn from consideration based on non-elected inventions as set forth in the restriction requirement.

Priority

5. This application is a national stage entry of 371 of PCT/EP00/06943 07/05/2000 which claims priority to (EPO) 99401764.8 07/13/1999.

Drawings

6. The drawings are objected to by the draftsperson under 37 C.F.R. 1.84 or 1.152. See PTO-948 for details.

Information Disclosure Statement

7. The Information Disclosure Statement submitted 1/11/02, paper # 3 has been signed and a signed copy of the same is attached here with the office action.

Specification - Informalities

8. Applicant should follow the direction or order or arrangement in framing the specification as provided in 37 CFR 1.77(b) since this is a utility application filed in USA. The specification should include all the sections in order. For example: Claims should begin with "I claim" or "'we claim" or "What is claimed is" and No Brief Description of Drawings are present in the application.

35 U.S.C. 112, first paragraph, requires the specification to be written in "full, clear, concise, and exact terms." The specification is replete with terms, which are not clear, concise and exact. The specification should be revised carefully in order to comply with 35 U.S.C. 112, first paragraph. Example of some unclear, inexact or verbose terms used in the specification is the Title" Neisseria meningitidis compounds and anti-**inflection** applications thereof" It should read as "Neisseria meningitidis compounds and anti-**infection** applications thereof" and on

pages 5, 6 16, 68, 69, 72, 73 and 78 the SEQ.ID.N° should be SEQ.ID.NO. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC 112, first paragraph

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-2, 5, 17 and 19 are rejected under 35 U.5.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is referred to the interim guidelines on written description published June 15, 1998 in the Federal Register at Volume 63, Number 114, pp 32639-32645 (also available at www.uspto.gov). This is a written description rejection.

The specification describes the FhaB polypeptide SEQ ID NO: 28 is encoded by a partial FhaB, 3' end polynucleotide sequence, SEQ.ID.NO: 27comprising 1047 nucleotides from *N. meningitidis* Z2491 strain. The actual biological function of the polypeptide, SEQ ID NO: 28 is not set forth in the specification. Applicants broadly describe an isolated polypeptide comprising an amino acid sequence which has at least 70% or 95%identity (fragments) to the amino acid sequence of SEQ.ID.NO: 28, obtained by embracing any substitution, insertion or deletion of amino acid throughout the entire stretch of polypeptide by use of language in which a fragment sequence that has % identity with SEQ.ID.NO: 28. These fragments do not meet the written

description provision of 35 U.S.C. 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she] invented what is claimed." (See Vas-Cath at page 1116.).

The actual structure or other relevant identifying characteristics of each fragment having the claimed properties of the polypeptide, SEQ.ID.NO: 28 can only be determined empirically by actually making every amino acid which can result in fragments with 70% or 95% identity to full length protein.

There must be some nexus between the structure of the polypeptide fragments and the function of that fragment. The specification fails to teach the structure or relevant identifying characteristics of said polypeptide fragments, sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed. With the exception of an isolated polypeptide comprising the amino acid sequence SEQ ID NO: 28, fragments that have 70% or 95% sequence identity are not adequately described. Written description requires more than a mere statement that it is part of the invention and reference to a potential method for making it. See Fiers v. Revel, 25 U5PQ2d 1601, 1606 (CAFC 1993) and Amgen Inc V Chugai Pharmaceutical Co Ltd., 18 U5PQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 U5PQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad

11. The rejection of claims 1- 2, 5, 17 and 19 are rejected under 35 U.5.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide comprising the amino acid sequence SEQ.ID.NO: 28, the specification does not reasonably

provide enablement for any isolated polypeptide that has at least 70% or 95% identity to SEQ ID NO: 28 (i.e., immunogenic fragments). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims is maintained as set forth in the previous office action.

The specification describes the FhaB polypeptide SEQ ID NO: 28 is encoded by a partial FhaB gene 3' end polynucleotide sequence, SEQ.ID.NO: 27comprising 1047 nucleotides from *N. meningitidis* Z2491 strain. The specification fails to indicate the biological activity of SEQ ID NO: 28, fails to teach that SEQ ID NO: 28, a polypeptide that is detected by immune or convalescent sera and further lacks any description of polypeptide SEQ ID NO: 28 which acts as a vaccine. The specification is not enabled for fragments because 1) the specification fails to teach that the alleged polypeptide fragments of SEQ ID NO: 28 is able to function as a vaccine composition 2) the specification fails to teach how to make and use fragments thereof that have an unknown and uncharacterized function; 3) the specification fails to teach what are the critical residues that can be modified and still achieve a fragment with any functional activity or any fragments with vaccine characteristics for Neisseria meningitidis; 4) the art teaches that polypeptides with replacement of single amino acid residues may lead to both structural and functional changes in biological activity and immunological recognition, one skilled in the art would have reason to doubt the validity and functionality of the function of the polypeptide of SEQ ID NO:28 as a vaccine and 5) applicants have not displayed a nexus between the structure of the amino acid sequence SEQ.ID.NO: 28 and function of the polypeptide as a vaccine. The actual biological function of the polypeptide, SEQ ID NO: 28 is not set forth in the specification.

As to points 1)- 5), the specification fails to provide a written description of any polypeptide comprising a fragment sequence that has at least 70% or 95% sequence identity to SEQ.ID.NO: 28. The specification fails to teach the critical polypeptide residues involved in the function of the polypeptide SEQ ID NO: 28, such that the skilled artisan is provided no guidance to test, screen or make fragments of the polypeptide comprising SEQ ID NO: 2 8or the polypeptide comprising SEQ ID NO: 28 using conventional technology which allow for a vaccine use in the specification. The specification fails to teach to what extent one could alter SEQ ID NO: 28 and still present the sequence as a vaccine. The specification also fails to demonstrate the actual biological function of the polypeptide and only assigns it as a polypeptide. Even if one were to use the in vivo vaccine methodology of the specification to screen for a vaccine, one of skill in the art would be reduced to merely randomly altering amino acid(s), which would lead to unpredictable results regarding the functional activity of the polypeptide to be used as a vaccine. Moreover, polypeptide chemistry is probably one of the most unpredictable areas of biotechnology and the art teaches that the significance of any particular amino acid and sequences for different aspects of biological activity can not be predicted a priori and must be determined empirically on a case by case basis (Rudinger et al, in "PEPTIDE HORMONES", edited by Parsons, J.A., University Park Press, June 1976, page 6). The art specifically teaches that even a single amino acid change in a polypeptide leads to unpredictable changes in the biological activity of the polypeptide. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological-activity of the polypeptide (Burgess et al., The Journal of Cell Biology, 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine, or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biologic activity of the mitogen

(Lazar et al., Molecular and Cellular Biology, 8(3): 1247-1252, 1988). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of a polypeptide. Polypeptides with replacement of a single amino acid residue may lead to both structural and functional changes in biological activity and immunological recognition. For example, Jobling et al. (Mol. Microbiol. 1991, 5(7): 1755-67 teaches a panel of single amino acid substitutions by oligonucleotide directed mutagenesis which products polypeptides that differ in native conformation, immunological recognition, binding and toxicity, thus exemplifying the importance of structural components to both biological function and immunological recognition. Applicants have not taught which residues of SEQ ID NO: 28 can be varied and still achieve a polypeptide that is functional as a vaccine. The specification has not conceived any other functionally equivalent polypeptide fragment and does not set forth the general tolerance to substitutions and where substitutions could be made. The lack of enabling description of make and use a polypeptide comprising a fragment sequence that has 70% or 95% sequence identity with SEQ.ID.NO: 28, the unpredictability associated with making and using the fragments of SEQ ID NO: 28 encompassed in the scope of the claims as set forth above, the lack of teaching even a beginning point for variation of the polypeptide sequence of SEQ ID NO: 28 for routine experimentation, lack of working examples commensurate in scope with the instant claims, the skilled artisan would be forced into undue experimentation.

12. Claims 1,17 and 19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement of a "vaccine composition" is considered to rest on a teaching of in vivo administration for purposes consistent with the intended use disclosed in the specification. The disclosed intended use for the claimed vaccine is for the treatment of otitis media and respiratory disease caused by *N.meningitidis* infections. Thus, the nature of the invention is a therapeutic vaccine composition used in the treatment or prevention. In addition, the instant specification does not teach how to use the composition, without undue experimentation, for the prevention, treatment, or cure of a disease in the animal to which the substance is administered. The specification discloses the claimed polypeptide is encoded by a partial FhaB, 3' end polynucleotide sequence comprising 1047 nucleotides from *N. meningitidis* Z2491 strain. There is insufficient guidance, which would enable one, skilled in the art to use the claimed compositions for their intended purpose, viz., for the generation of a protective immune response against disease caused by *N. meningitidis* infections. At the time the invention was made, vaccines to serogroup B (specification page 2) appears to be still at experimental stage as it shares structural similarity to host components and more work is needed for an effective vaccine to serogroup B becomes available. The specification does not teach the immunogenicity of the claimed composition. The specification lacks guidance by way of general methods or working examples which teach an "effective amount" of the vaccine which would be used for this purpose. Lack of working examples is given added weight in cases involving an unpredictable and undeveloped art, such as immunotherapy of respiratory diseases caused by *N. meningitidis* It is unpredictable whether the claimed composition, which is disclosed as being only immunogenic, would have the added property of generating the protective immune response sufficient to inhibit the diseases causes by *N. meningitidis* because the state of the art discloses that vaccine development to serogroup B isolates were unsuccessful and polysaccharide vaccines are currently being improved (specification page 2). Therefore, testing

the claimed polypeptides in animal models or clinical testing of these antigens is critical. The specification has not disclosed a link or nexus between the generation protective immunity using the claimed peptide and its use in preventing the *N. meningitidis* infections. Accordingly, there is no objective basis upon which the skilled artisan would reasonably be able to determine or predict an amount of the claimed composition/vaccine effective for its intended use. Therefore, undue experimentation would be required to make and use the invention.

Claim Rejections - 35 USC 112, second paragraph

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

14. Claims 4 and 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 is rejected as being vague for the recitation of "substantially." As written it is impossible to understand the metes and bounds of the term substantially.

Claim 4 is rejected as being vague for the recitation of "isolated polypeptide of". Does applicant intend to mean an isolated polypeptide consisting of SEQ.ID.NO: 28?

Claim Rejections - 35 USC 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 1-5, 17 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Martin et al 1997 (J.Ex.Med. Volume 185, Number 7, April 7, 1997 1173-1184).

Claims are directed to an isolated polypeptide or vaccine comprising an amino acid sequence an amino acid sequence SEQ.ID.NO: 28 or immunogenic fragments of said polypeptide and a pharmaceutically acceptable carrier.

Martin et al disclose an isolated polypeptide, outer membrane protein from whole cell lysate of OM preparations from various clinical isolated including nine meningococcal strains (page 1174, under materials and method, antigens). Applicant's use of the open-ended term "comprising " in the claims fails to exclude unrecited steps or ingredients and leaves the claims open for inclusion of unspecified ingredients, even in major amounts. Whole cell lysates prepared in buffer (pharmaceutical carrier) from N.meningitidis inherently comprise the amino acid sequence as set forth in the SEQ.ID.NO: 28 and several N.meningitidis antigens. See In re Horvitz, 168 F 2d 522, 78 U.S.P.Q. 79 (C.C.P.A. 1948) and Ex parte Davis et al., 80 U.S.P.Q. 448 (PTO d. App. 1948). In the absence of evidence to the contrary the disclosed prior art protein and the claimed isolated polypeptide comprising SEQ.ID.NO: 28 are the same. Since the Office does not have the facilities for examining and comparing applicants' claimed isolated polypeptide comprising SEQ.ID.NO: 28, with the polypeptide of prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. . It is acknowledged that weight is given to every term in claims 17 and 19. This is why the instant claims drawn to immunogenic composition i.e., vaccine is scrutinized differently from a composition claim under 112, first paragraph. However, under prior art rejections, the term vaccine must be weighed with the structural limitations of the claim. If the immunogenic composition i.e., vaccine merely comprises a known composition, the term carries little weight absent evidence of structural difference. Of course, the existence of an unobvious

structural difference would define over the prior art. Here, the prior art teaches the same composition as claimed. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594

Status of Claims

17. No claims are allowed.

Conclusion

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padma Baskar whose telephone number is (703) 308-8886. The examiner can normally be reached on Monday through Friday from 6:30 AM to 4 PM EST

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Padma Baskar Ph.D.

11/11/03

MARK NAVARRO
PRIMARY EXAMINER